Remarks

I. Introduction

Claims 1 to 31 are pending in the present application. In view of the foregoing amendment, it is respectfully submitted that all of the presently pending claims are allowable, and reconsideration is respectfully requested.

II. Rejection of Claims 1-7, 12-23 and 26-31 Under 35 U.S.C. §103(a)

Claims 1-7, 12-23 and 26-31 were rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 6,110,384 ("Goux et al.") in view of U.S. Patent No. 6,258,027 ("Sternby et al."). Applicant respectfully submits these claims are not obvious over the combination of Goux et al. and Sternby et al., and requests that the §103(a) rejections be withdrawn.

Claim 1 relates to a method for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment, in which the blood to be treated flows in an extracorporeal circuit through the blood chamber of a dialyzer subdivided by a semipermeable membrane into the blood chamber and a dialyzing-fluid chamber, and dialyzing fluid flows in a dialyzing-fluid path through the dialyzing-fluid chamber of the dialyzer. Claim 1 recites that the method includes the step of bringing about a change in the concentration of a blood component in the blood upstream of the dialyzer by a change in a physical or chemical characteristic in the dialyzing fluid upstream of the dialyzer. Claim 1 recites that the method also includes the step of measuring the change in the physical or chemical characteristic in the dialyzing fluid downstream of the dialyzer which can be attributed to the change in the concentration of the blood component in the blood. Claim 1 recites that the method further includes the step of determining the distribution volume V of the blood component from the change in the physical or chemical characteristic in the dialyzing fluid upstream and downstream of the dialyzer.

Claim 2 relates to a method for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment, in which the blood to be treated flows in an extracorporeal circuit through the blood chamber of a dialyzer subdivided by a semipermeable membrane into the blood chamber and a dialyzing-fluid chamber, and dialyzing fluid flows in a dialyzing-fluid path through the dialyzing-fluid chamber of the dialyzer. Claim 2 recites that a physical or chemical characteristic of the dialyzing fluid is altered in the dialyzing-fluid path upstream of the dialyzer, and the physical or chemical characteristic of the dialyzing fluid is measured downstream of the dialyzer. Claim 2 has been amended herein without prejudice to recite that the change as a function of time in the concentration of a blood component in the blood upstream of the dialyzer Δcbi is determined from the physical or chemical characteristic of the dialyzing fluid upstream and downstream of the dialyzer after the physical or chemical characteristic of the dialyzing fluid

has been altered. Support for this amendment can be found at page 7, lines 1-3, which states that "[t]he physical or chemical characteristic of the dialyzing fluid is altered in the dialyzing-fluid path upstream from the dialyzer," and at page 7, lines 12-15 which states that "[t]he change in the concentration of the blood component in the blood as a function of time is determined from the physical or chemical characteristic of the dialyzing fluid downstream of the dialyzer." Claim 2 recites that the distribution volume V of the blood component is determined from the change as a function of time in the concentration of a blood component in the blood.

Claim 12 relates to an apparatus for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment in conjunction with an extracorporeal blood-treatment device, in which the blood to be treated flows in an extracorporeal circuit through the blood chamber of a dialyzer subdivided by a semipermeable membrane-into the blood chamber and a dialyzing-fluid chamber, and dialyzing fluid flows in a dialyzing-fluid path through the dialyzing-fluid chamber of the dialyzer. Claim 12 recites that the apparatus includes a device for altering the physical or chemical characteristic of the dialyzing fluid in the dialyzing-fluid path upstream of the dialyzer. Claim 12 recites that the apparatus includes a measuring device for determining the physical or chemical characteristic of the dialyzing fluid in the dialyzing-fluid path downstream of the dialyzer. Claim 12 recites that the apparatus includes an arithmetic and evaluation unit which is designed in such a way that the distribution volume V of the blood component can be determined from a change in the physical or chemical characteristic in the dialyzing fluid downstream of the dialyzer which can be attributed to the change in the concentration of a blood component in the blood because of a change in the physical or chemical characteristic in the dialyzing fluid upstream of the dialyzer.

Claim 13 relates to an apparatus for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment in conjunction with an extracorporeal blood-treatment device, in which the blood to be treated flows in an extracorporeal circuit through the blood chamber of a dialyzer subdivided by a semipermeable membrane into the blood chamber and a dialyzing-fluid chamber, and dialyzing fluid flows in a dialyzing-fluid path through the dialyzing-fluid chamber of the dialyzer. Claim 13 recites that the apparatus includes a device for altering the physical or chemical characteristic of the dialyzing fluid in the dialyzing-fluid path upstream of the dialyzer. Claim 13 recites that the apparatus includes a measuring device for determining the physical or chemical characteristic of the dialyzing fluid in the dialyzing-fluid path downstream of the dialyzer. Claim 13 has been amended herein without prejudice to recite that the apparatus includes an arithmetic and evaluation unit which is designed in such a way that the change as a function of time in the concentration of the blood component Δcbi in the blood upstream of the dialyzer can be determined from the physical or chemical characteristic

of the dialyzing fluid upstream and downstream of the dialyzer after the physical or chemical characteristic of the dialyzing fluid has been altered, and the distribution volume V of the blood component can be determined from the change as a function of time in the concentration of the blood component upstream of the dialyzer. Support for this amendment is set forth above in connection with claim 2.

Goux et al. purport to disclose a method for determining a parameter - D (dialysance), K (clearance), Kt/v (clearance multiplied by treatment time and divided by the volume of distribution of urea), Cbin (concentration of sodium in a patient's bloodstream upstream of a hemodialyser) - indicative of the effectiveness of an extracorporeal blood treatment carried out using a membrane exchanger. Goux et al. state that the method includes the steps of flowing through the exchanger a treatment liquid having a concentration characteristic (Cd) and of varying the value of the characteristic (Cd) upstream of the exchanger for a time at the end of which the characteristic (Cd) is returned to a nominal value. Goux et al. also state that a plurality of values adopted by the characteristic (Cd) downstream of the exchanger in response to the upstream variation is measured and stored in memory. Goux et al. also state that the area (Sout) of a downstream perturbation region is determined, which is bounded by a baseline and a curve representing the variation of the measured values with respect to time. Furthermore, Goux et al. state that the parameter (D, K, Kt/v, Cbin) indicative of the effectiveness of the treatment is calculated using the area (Sin) beneath the upstream curve and an area beneath a downstream curve.

Sternby et al. purports to relate to a method and apparatus for calculating a parameter of mass exchange of a solute fluid including passing the solute in a predetermined volume of the fluid on one side of a semi-permeable membrane in a dialyzer, passing an exchange fluid on the other side of the semi-permeable membrane, obtaining a concentration curve by repeatedly measuring the concentration of a solute such as urea in the mass exchange fluid, fitting an approximate curve having a logarithm comprising a substantially straight line with at least a portion of a concentration curve, determining a parameter of the approximation curve, and calculating the mass of urea in the predetermined volume of fluid by the formula $m=(Q_d.x.c_d)/P$ where m is the mass of the urea, Q_d is the flow rate of the exchange fluid, C_d is the concentration of the urea in the exchange fluid, and P is the parameter.

The Final Office Action states that "Goux discloses a method of determining a parameter of extracorporeal blood treatment that includes the steps claimed by applicant." Final Office Action at page 2. The Final Office Action states that "[i]n particular, Goux discloses that the blood flows through one side of the dialyzer loop, with treatment fluid through the second side of the loop." Final Office Action at page 2. The Final Office Action states that "[w]hile the treatment fluid flows through the treatment side of the loop, the operator varies the value of a component in the stream of treatment fluid upstream of the

dialyzer, measuring the value of the component downstream of the dialyzer, and calculating the parameter indicative of the treatment." Final Office Action at page 2. The Final Office Action states that "[s]uch a calculation may include a calculation of a substance in the patient's blood. See columns 2-4." Final Office Action at page 2. The Final Office Action states that "[t]he system comprises a conductivity sensors 23 and 25 both upstream and downstream of the dialyzer for taking measurements, a syringe driver for altering the characteristic of the dialyzing fluid, and computing a control unit 30." Final Office Action at page 2. The Final Office Action admits that "Goux fails to disclose that the Kt/V measurement obtained in his method can be used to extrapolate V, the distribution volume of a substance in the patient's blood." Final Office Action at page 2. However, the Final Office Action states that "Sternby discloses a method whereby measurements are taken from the blood side and diasylate side in an extracorpoeal treatment, and the values extrapolated to determine V, the distribution volume of a substance in the blood, an important clinical measurement to determine the parameters of patient treatment (see columns 17-19)." Final Office Action at page 3. The Final Office Action concludes that "it would have been obvious to one of ordinary skill in the art at the time of invention to use the method of taking measurements disclosed by Goux and using those measurements to extrapolate the distribution volume of a substance in the patient blood in order to determine and adjust patient treatment, as taught by Sternby." Final Office Action at page 3.

Applicants respectfully contend that claims 1, 2, 12 and 13 are not obvious over the combination of Goux et al. and Sternby et al. for at least the reason that the combination of Goux et al. and Sternby et al. do not disclose each and every element of claims 1, 2, 12 and 13. For instance, the combination of Goux et al. and Sternby et al. fail to disclose or even suggest an apparatus or method for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment that includes determining the distribution volume V of a blood component from a change in a physical or chemical characteristic in the dialyzing fluid upstream and downstream of the dialyzer, as recited in claims 1 and 12, nor an apparatus or method for determining the distribution volume of a blood component in the body of an organism during an extracorporeal blood treatment that includes determining the distribution volume V of a blood component from the change as a function of time in the concentration of a blood component in the blood after the physical or chemical characteristic of the dialyzing fluid has been altered, as recited in claims 2 and 13. Instead, Goux et al. purports to "provide[ ] a method of determining a parameter (D, K, Kt/v, Cbin) indicative of the effectiveness of an extracorporeal treatment of blood." Column 2, lines 50 to 53. None of the parameters determined by Goux et al., i.e., D (dialysance), K (clearance), Kt/v (clearance multiplied by treatment time and divided by the volume of distribution of urea) and Cbin (concentration of sodium in a patient's bloodstream upstream of a hemodialyser), constitute the distribution

volume of a blood component in the body of an organism during an extracorporeal blood treatment. To the extent that the determination in Goux et al. of the parameter Kt/v includes the volume of distribution of urea (v), Goux et al. provide no teaching or suggestion regarding how to actually determine the volume of distribution of urea (v) in the body of an organism during an extracorporeal blood treatment, since it is the clearance K that is determined by the process of Goux et al. The Final Office Action admits that "Goux et al. fail to disclose that the Kt/V measurement obtained in his method can be used to extrapolate V, the distribution volume of a substance in the patient's blood." Final Office Action at page 2.

Moreover, Sternby et al. state that "[s]ince the plasma water concentration of urea can be calculated as indicated above and the amount of urea at the start of the treatment is estimated according to the present invention, the distribution volume V of urea in the body can be calculated." Col. 20, lines 32-34. Thus, to the extent that Sternby et al. describes that a distribution volume of urea in the body can be calculated, Sternby et al. requires that a plasma water concentration of urea be calculated according to Equation 27 (see col. 20, lines 20-28), and that the amount of urea at the start of the treatment be estimated, rather than determining a distribution volume of a blood component from a change in a physical or chemical characteristic in the dialyzing fluid upstream and downstream of the dialyzer, or from a change as a function of time in the concentration of a blood component in the blood after a physical or chemical characteristic of the dialysing fluid has been altered.

As set forth above, the Final Office Action states that "Sternby discloses a method whereby measurements are taken from the blood side and diasylate side in an extracorpoeal treatment, and the values extrapolated to determine V, the distribution volume of a substance in the blood, an important clinical measurement to determine the parameters of patient treatment (see columns 17-19)." Final Office Action at pages 2-3. The Final Office Action also states that "the Sternby reference is used only to demonstrate that, given the value of other variables in the equation Kt/V, it would have been obvious to one of ordinary skill in the art at the time of invention to complete the algebraic equation to determine the volume of distribution of urea in the body." Final Office Action at pages 3-4, emphasis added. However, the combination of these two references would not teach or suggest how to actually determine the volume of distribution of urea (v) in the body of an organism during an extracorporeal blood treatment, because irrespective of whether Sternby discloses that the value of measurements taken from the blood side and diasylate side in an extracorpoeal treatment may be extrapolated to determine V, the distribution volume of a substance in the blood, Sternby extrapolates using a different formula than that disclosed by Goux et al.

In rejecting a claim under 35 U.S.C. § 103(a), the Examiner bears the initial burden of presenting a prima facie case of obviousness. In re Rijckaert, 9 F.3d 1531, 1532, 28 U.S.P.Q.2d 1955, 1956 (Fed. Cir. 1993). To establish prima facie obviousness, three

criteria must be satisfied. First, there must be some suggestion or motivation to modify or combine reference teachings. In re Fine, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). This teaching or suggestion to make the claimed combination must be found in the prior art and not based on the application disclosure. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). Second, there must be a reasonable expectation of success. In re Merck & Co., Inc., 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). Third, the prior art reference(s) must teach or suggest all of the claim limitations. In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). As more fully set forth above, it is respectfully submitted that the combination of Goux et al. and Sternby et al. does not disclose, or even suggest, all of the features recited in claims 1, 2, 12 and 13.

Moreover, it is respectfully submitted that the cases of In re Fine, supra, and In re Jones, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992), make plain that the Final Office Action's generalized assertions that it would have been obvious to modify the reference do not properly support a § 103 rejection. It is respectfully submitted that those cases make plain that the Final Office Action reflects a subjective "obvious to try" standard, and therefore does not reflect the proper evidence to support an obviousness rejection based on the references relied upon. In particular, the Court in the case of In re Fine stated that:

> The PTO has the burden under section 103 to establish a *prima facie* case of obviousness. It can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. This it has not done. . . .
>
> **Instead, the Examiner relies on hindsight in reaching his obviousness determination. . . . One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.**

In re Fine, 5 U.S.P.Q.2d at 1598 to 1600 (citations omitted; italics in original; emphasis added). Likewise, the Court in the case of In re Jones stated that:

> Before the PTO may combine the disclosures of two or more prior art references in order to establish *prima facie* obviousness, there must be some suggestion for doing so, found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. . . .
>
> **Conspicuously missing from this record is any evidence, other than the PTO's speculation (if it be called evidence) that one of ordinary skill . . . would have been motivated to make the modifications . . . necessary to arrive at the claimed [invention].**

In re Jones, 21 U.S.P.Q.2d at 1943, 1944 (citations omitted; italics in original).

That is exactly the case here since it is believed and respectfully submitted that the present Final Office Action offers no evidence whatsoever, but only conclusory hindsight, reconstruction and speculation, which these cases have indicated does not constitute evidence that will support a proper obviousness finding. Unsupported assertions are not evidence as to why a person having ordinary skill in the art would be motivated to combine or modify the references to provide the claimed subject matter of the claims to address the problems met thereby. Accordingly, the Office must provide proper evidence of a motivation for combining or modifying the references to provide the claimed subject matter.

More recently, the Federal Circuit in the case of In re Kotzab has made plain that even if a claim concerns a "technologically simple concept" — which is not the case here — there still must be some finding as to the "specific understanding or principle within the knowledge of a skilled artisan" that would motivate a person having no knowledge of the claimed subject matter to "make the combination in the manner claimed," stating that:

> In this case, the Examiner and the Board fell into the hindsight trap. The idea of a single sensor controlling multiple valves, as opposed to multiple sensors controlling multiple valves, is a technologically simple concept. With this simple concept in mind, the Patent and Trademark Office found prior art statements that in the abstract appeared to suggest the claimed limitation. But, there was no finding as to the specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of Kotzab's invention to make the combination in the manner claimed. In light of our holding of the absence of a motivation to combine the teachings in Evans, we conclude that the Board did not make out a proper prima facie case of obviousness in rejecting [the] claims . . . under 35 U.S.C. Section 103(a) over Evans.

In re Kotzab, 55 U.S.P.Q.2d 1313, 1318 (Fed. Cir. 2000) (emphasis added). Again, it is believed that there have been no such findings.

Thus, for at least this reason, the combination of Goux et al. and Sternby et al. fails to disclose or suggest each and every feature of the claims 1, 2, 12 and 13, and the rejection of claims 1, 2, 12 and 13 should be withdrawn. In addition, claims 3-7 which depend from and therefore include all of the limitations of claim 1, claims 23-23 which depend from and therefore include all of the limitations of claim 2, claims 14-21 which depend from and therefore include all of the limitations of claim 12, and claims 26-31 which depend from and therefore include all of the limitations of claim 13, should be deemed allowable for at least the same reasons, and the rejection of these claims should be withdrawn also.

III. Allowed Subject Matter

Applicants gratefully acknowledge that claims 8 to 11, 24 and 25 are indicated to be allowed.

IV. Fees

Any additional fees or charges required at this time in connection with this application may be charged to Patent and Trademarks Office Deposit Account No. 11-0600.

V. Conclusion

It is therefore respectfully submitted that all of the presently pending claims are allowable. All issues raised by the Examiner having been addressed, an early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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